

Sprouts of the broccoli cultivar Everest contained 130-fold more inducer potential (units/g fresh weight) than mature vegetables. The inducer activity in broccoli was significantly higher than in daikon.

5

CL  
Example 5

CL<sup>u</sup>/ INDUCER POTENTIAL OF BROCCOLI SPROUT EXTRACTS

Inducer potential of a series of water extracts of 3-day old broccoli sprouts of the cultivar Saga were determined. Plants were prepared by first surface sterilizing seeds of *Brassica oleracea* variety *italica* (broccoli) cultivar Saga by a 1 min treatment in 70% ethanol, followed by 15 min in 1.3% sodium hypochlorite containing approximately 0.001% Alconox detergent. Seeds were grown in sterile plastic containers at a density of approximately 8 seeds/cm<sup>2</sup> for 72 hours on a 0.7% agar support that did not contain added nutrients. The environment was carefully controlled with broad spectrum fluorescent lighting, humidity and temperature control (16 hours light, 25°C / 8 hours dark, 20°C).

Plants were rapidly and gently collected from the surface of the agar to minimize glucosinolate hydrolysis by endogenous myrosinase released upon plant wounding. Sprouts (approximately 25 mg fresh wt/sprout) were gently harvested and immediately and rapidly plunged into approximately 3 volumes of boiling water in order to inactivate endogenous myrosinase as well as to extract glucosinolates and isothiocyanates from the plant tissue. Water was returned to a boil and maintained at a rolling boil for 3 min. The sprouts were then either strained from the boiled infusion [tea, soup] or homogenized in it, and the residue then removed by filtration or centrifugation.

Data in Table 3 represent both homogenates and infusions. Preparations were stored at -20°C until assayed. Inducer potential of plant extracts, prepared

29

as described above, was determined as described in Definitions section above.

4T,0300X

TABLE 3  
Inducer Potentials of Hot Water Extracts  
of 3-Day Saga Broccoli Sprouts

5

EXTRACT NO.	units/g fresh weight
1	500,000
2	370,000
3	455,000
4	333,000
5	435,000
6	333,000
7	625,000
8	250,000
9	313,000
10	357,000
11	370,000
12	370,000
13	217,000
14	222,000
15	1,000,000
16	714,000
17	435,000
18	1,250,000
19	263,000
AVERAGE	464,000 $\pm$ 61,600 S.E.M.

10

15

20

25

86022012988T60

30

30

Some variability in the amount of Phase 2 enzyme-inducer potential was detected. High levels of Phase 2 enzyme-inducer potential, however, were consistently observed.

5

CL  
CLV/L **Example 6**  
**HOT WATER BROCCOLI EXTRACTS TREATED**  
**WITH DAIKON MYROSINASE**

QR activity in a hot water broccoli extract increased in the presence of a vegetable source of myrosinase. An aqueous extraction of 3-day old sprouts of broccoli cultivar Saga grown on water agar, in which myrosinase was inactivated by boiling for 3 min, was divided into 6 different 150 ml aliquots. Nine-day old daikon sprouts, a rich source of the enzyme myrosinase, were added to this cooled infusion in amounts equivalent to 0, 5, 9, 17, 29 and 40% (w/w) of the broccoli. QR activity, as determined in the Definition section, of the control extracts containing 0% daikon was 26,300 units/gram fresh weight while QR activity of the extracts that had received daikon as a source of myrosinase ranged from 500,000 to 833,000 units/gram fresh weight of broccoli. Accordingly, myrosinase present in the daikon sprouts, increased the QR activity in the broccoli extract greater than 19-fold.

25

CL  
CLV/L **Example 7**  
**GLUCORAPHANIN AND GLUCOERUCIN ARE THE PREDOMINANT**  
**GLUCOSINOLATES IN HOT WATER EXTRACTS OF BROCCOLI**  
**(CULTIVAR SAGA) SPROUTS**

Paired Ion Chromatography (PIC). Centrifuged hot water extracts of 3-day-old broccoli (cultivar Saga) sprouts were subjected to analytical and preparative PIC on a reverse phase C18 Partisil ODS-2 HPLC column in ACN/H<sub>2</sub>O (1/1, by vol.) with tetraoctylammonium (TOA) bromide as the counter-ion. Only three well-separated peaks were detected: peak A eluted at 5.5 min, B at 11.5

31

min, and C at 13 min at a molar ratio [A:B:C] of ca. 2.5 : 1.6 : 1.0 (monitored by UV absorption at 235 nm), and they disappeared if the initial extracts were first treated with highly purified myrosinase. Peaks A, B, and C contained no significant inducer activity, and cyclocondensation assay of myrosinase hydrolysates showed that only Peaks A and C produced significant quantities of isothiocyanates, accounting for all the inducer activity. See Zhang et al., *Anal. Biochem.* 205: 100-107 (1992). Peak B was not further characterized. Peaks A and C were eluted from HPLC as TOA salts but required conversion to ammonium salts for successful mass spectroscopy, NMR and bioassay. The pure peak materials were dried in a vacuum centrifuge, redissolved in aqueous 20 mM  $\text{NH}_4\text{Cl}$ , and extracted with chloroform to remove excess TOA bromide. The ammonium salts of glucosinolates remained in the aqueous phase, which was then evaporated.

*Identification of Glucosinolates.* The ammonium salts of Peaks A and C were characterized by mass spectrometric and NMR techniques: (a) negative ion Fast Atom Bombardment (FAB) on a thioglycerol matrix; this gave values of 436 (Peak A) and 420 (Peak C) amu for the negative molecular ions, and (b) high resolution NMR, as shown in Figure 2, provided unequivocal identification of the structure. Peak A is glucoraphanin [4-methylsulfinylbutyl glucosinolate], and Peak C is the closely related glucoerucin [4-methylthiobutyl glucosinolate]. These identifications and purity are also consistent with the inducer potencies; Peaks A and C, after myrosinase hydrolysis had potencies of 36,100 and 4,360 units/ $\mu\text{mol}$ , respectively, compared with reported CD values of 0.2  $\mu\text{M}$  (33,333 units/ $\mu\text{mol}$ ) for sulforaphane and 2.3  $\mu\text{M}$  (2,900 units/ $\mu\text{mol}$ ) for erucin. CD values are the concentrations of a compound required to double the QR specific activity in Hepa 1c1c7 murine hepatoma cells. Since there are no other glucosinolate peaks, and the inducer activity of peak A and C account for the total inducer activity of the extracts, it is

32

therefore likely that in this cultivar of broccoli, there are no significant quantities of other inducers, i.e., no indole or hydroxyalkenyl glucosinolates. Further, the isolated compounds are therefore substantially pure.

5

CLV/L

CL

**Example 8****COMPARISON OF AQUEOUS AND ORGANIC SOLVENT TECHNIQUES  
FOR EXTRACTION OF INDUCER POTENTIAL**

Plants were prepared by first surface sterilizing seeds of *Brassica oleracea* variety *italica* (broccoli) cultivar Saga, with 70% ethanol followed by 1.3% sodium hypochlorite and 0.001%alconox. The seeds were grown in sterile plastic containers at a density of approximately 8 seeds/cm<sup>2</sup> for 72 hours on a 0.7% agar support that did not contain added nutrients. The environment was carefully controlled with broad spectrum fluorescent lighting, humidity, and temperature control (16 hours light, 25°C/8 hours dark, 20°C).

The plants were rapidly and gently collected from the surface of the agar to minimize glucosinolate hydrolysis by endogenous myrosinase released upon plant wounding. A portion of the plants was homogenized with 10 volumes of the DMF/ACN/DMSO solvent at -50°C, as described in Example 1, which dissolves nearly all the non-lignocellulosic plant material. Alternatively, the bulk of the harvested plants was plunged into 5 volumes of boiling water for 3 min to inactivate endogenous myrosinase and to extract glucosinolates and isothiocyanates. The cooled mixture was homogenized, centrifuged, and the supernant fluid was stored at -20°C.

Inducer potential of plant extracts, prepared by the two methods described above, was determined by the microtiter plate bioassay as described above. Typical inducer potentials in an average of 5 preparations were 702,000 (DMF/ACN/DMSO extracts) and 505,000 (aqueous extracts) units/g fresh weight of sprouts.

33

Spectrophotometric quantitation of the cyclocondensation product of the reaction of isothiocyanates with 1,2-benzenedithiole was carried out as described in Zhang et al., *Anal. Biochem.* 205: 100-107 (1992). Glucosinolates were rapidly converted to isothiocyanates after addition of myrosinase. About 6% of the total hot water extractable material [dissolved solids] consisted of glucosinolates. These results demonstrate that (a) isothiocyanate levels in the crude plant extracts are extremely low; (b) myrosinase rapidly converts abundant glucosinolates to isothiocyanates; (c) hot water extraction releases over 70% of the inducer activity extractable with a triple solvent mixture permitting recovery of most of the biological activity in a preparation that is safe for human consumption; and (d) over 95% of the inducing potential in the intact plant is present as glucosinolates and therefore no other inducers are present in biologically significant quantities.

CL

**Example 9**

20 CL<sup>1/2</sup> **DEVELOPMENTAL REGULATION OF GLUCOSINOLATE PRODUCTION**

Preliminary experiments in which field grown broccoli (cultivar DeCicco) was harvested at sequential time points from the same field indicated that on a fresh weight basis, inducer potential declined from the early vegetative stage through commercial harvest, but appeared to increase at late harvest (onset of flowering). These data suggested that inducer potential might be highest in seeds. Subsequent studies have shown that when seeds of 8 broccoli cultivars were surface sterilized and grown under gnotobiotic conditions, Phase 2 enzyme-inducer potential was highest in seeds and declined progressively (on a fresh weight basis) over time throughout the first 14 days of seedling growth.

Expressed on a per plant basis, however, activity remained constant over this period, suggesting that at

5 this early stage of growth there was no net synthesis of glucosinolates. However, when the glucosinolate profiles of market stage broccoli heads and 3 day old sprouts (cultivar Emperor) were compared, there was a profound difference in the apparent glucosinolate compositions of these plants.

10 Sprouts were prepared by first surface sterilizing seeds of *Brassica oleracea* variety *italica* (broccoli) cultivar Emperor with a 1 minute treatment in 70% ethanol, followed by 15 min in 1.3% sodium hypochlorite with approximately 0.001% Alconox detergent. Seeds were grown in sterile plastic containers at a density of approximately 8 seeds/cm<sup>2</sup> for 72 hours on a 0.7% agar support that did not contain added nutrients. The  
15 environment was carefully controlled; broad spectrum fluorescent lighting, humidity and temperature control (16 hours light, 25°C / 8 hours dark, 20°C).

20 Plants were rapidly and gently collected from the surface of the agar to minimize glucosinolate hydrolysis by endogenous myrosinase released upon plant wounding. Sprouts [approximately 25 mg fresh wt/sprout], were gently harvested and immediately and rapidly plunged into approximately 3 volumes of boiling water in order to inactivate endogenous myrosinase as well as to extract  
25 glucosinolates and isothiocyanates from the plant tissue. Water was returned to a boil and maintained at a rolling boil for 3 min. The sprouts were then strained from the boiled infusion [tea, soup] and the infusion was stored at -20°C until assayed.

30 Market stage heads were obtained by germinating seeds of the same seedlot in a greenhouse in potting soil, transplanting to an organically managed field in Garrett County, MD and harvested at market stage. Heads were immediately frozen upon harvest, transported to the  
35 laboratory on ice and extracts were prepared in an identical fashion to those described above for sprouts

35

35

except that approximately 3 gram floret tissue samples were used for extraction.

Inducer potential of plant extracts, prepared as described above, was determined by the microtiter plate bioassay method as described in Example 1. Paired ion chromatography revealed two major peaks, probably glucobrassicin and neo-glucobrassicin, in extracts of market stage heads with similar retention times to glucobrassicin (indole-3-ylmethyl glucosinolate) and neo-glucobrassicin (1-methoxyindole-3-ylmethyl glucosinolate). This observation is consistent with published reports on the glucosinolate composition of mature broccoli plants. However, paired ion chromatography under the same conditions of identically prepared extracts of 3-day-old sprouts showed absence of glucobrassicin or neo-glucobrassicin. Additionally, 3-day-old sprouts of different broccoli cultivars produce different mixtures of glucosinolates. Accordingly, glucosinolate production is developmentally regulated.

20

CL  
CL<sup>u</sup>/L

**Example 10**  
**EVALUATION OF ANTICARCINOGENIC ACTIVITIES**  
**OF BROCCOLI SPROUT PREPARATIONS IN THE HUGGINS**  
**DMBA (9,10 DIMETHYL-1,2-BENZANTHRACENE)**  
**MAMMARY TUMOR MODEL**

25

Sprouts were prepared by first surface sterilizing seeds of *Brassica oleracea* variety *italica* (broccoli) cultivar Saga with a 1 min treatment in 70% ethanol, followed by 15 min in 1.3% sodium hypochlorite with approximately 0.001% Alconox detergent. Seeds were grown in sterile plastic containers at a density of approximately 8 seeds/cm<sup>2</sup> for 72 hours on a 0.7% agar support that did not contain added nutrients. The environment was carefully controlled with broad spectrum fluorescent lighting, humidity and temperature control (16 hours light, 25°C / 8 hours dark, 20°C).

30

35

36



09110867, 072008

The plants were rapidly and gently collected from the surface of the agar to minimize glucosinolate hydrolysis by endogenous myrosinase released upon plant wounding. A large quantity of sprouts was harvested by immediately and rapidly plunging into approximately 3 volumes of boiling water in order to inactivate endogenous myrosinase, as well as extracting glucosinolates and isothiocyanates from the plant tissue. Water was returned to a boil and maintained at a rolling boil for 3 min. Sprouts were then strained from the boiled infusion [tea, soup] and the infusion was lyophilized and stored as a dry powder at -20°C [designated Prep A]. Other sprouts, similarly prepared were extracted with boiling water, cooled to 25°C and were amended with a quantity of 7 day old daikon sprouts equivalent to approximately 0.5% of the original fresh weight of broccoli sprouts. This mixture was homogenized using a Brinkman Polytron Homogenizer and incubated at 37°C for 2 hours following which it was filtered through a sintered glass filter, lyophilized as above and stored as a dried powder at -20°C [designated Prep B].

QR inducer activity and inducer potential of plant extracts, prepared as described above, was determined by the microtiter plate bioassay method as described above. The induction of QR activity in preparation A is largely due to glucosinolates; predominantly glucoraphanin, which is the glucosinolate of sulforaphane, but this preparation also contains some glucoerucin, which is the sulfide analog of glucoraphanin. The induction QR activity of preparation B is almost exclusively due to isothiocyanates arising from treatment of glucosinolates with myrosinase.

Female Sprague-Dawley rats received at 35 days of age were randomized; 4 animals per plastic cage. All animals received 10 mg DMBA, by gavage in 1 ml sesame oil, at age 50 days. Sprout preparations (A or B) or vehicle control were given by gavage at 3, 2 & 1 day prior to DMBA, on

37

37

the day of DMBA (2 hr prior to the DMBA dose) and on the  
day following DMBA dosing. The vehicle used was 50%  
Emulphor 620P / 50% water. Animals were maintained on a  
semi-purified AIN-76A diet *ad libitum* from the time of  
5 receipt until termination of the experiment (167 days of  
age).

00118867-072098

38

860220-12988TT60

T10390X

38

TABLE 4

**ANTICARCINOGENIC ACTIVITIES OF BROCCOLI SPROUT EXTRACTS  
IN THE DMBA RAT MAMMARY TUMOR MODEL**

GROUP	TREATMENT	NUMBER OF ANIMALS AT TERMINATION	TOTAL TUMOR NUMBER	MULTIPLICITY: NUMBER OF TUMORS PER RAT
CONTROL	DMBA only	19	34	1.79
PREPARATION A (Glucosinolate)	324 mg/dose (100 $\mu$ mol sulforaphane equiv.)	18	19	1.05
PREPARATION B (Isothiocyanate)	424 mg/dose (100 $\mu$ mol sulforaphane equiv.)	20	11	0.55

5

10

39

The development of palpable tumors was delayed for as much as 5 weeks by the administration of sprout extracts. Rats treated with either Preparation A or B had significantly fewer tumors than the untreated control, and the multiplicity of tumors (tumors per rat) was significantly lower in the animals receiving Preparations A or B.

CL  
CL<sup>U</sup>/L **Example 11**  
**METABOLISM AND CLEARANCE OF GLUCOSINOLATES IN HUMANS**

Two male, non-smoking volunteers ages 35 and 40 years, each in good health, were put on a low vegetable diet in which no green or yellow vegetables, or condiments, mustard, horseradish, tomatoes or papayas were consumed. After 24 hours on such a diet, all urine was collected in 8 hr aliquots. After 24 hours of baseline data, subjects ingested 100 ml of broccoli sprout soup (prepared as below), containing 520  $\mu$ mol of glucosinolates.

The sprouts were prepared by first surface sterilizing seeds of *Brassica oleracea* variety *italica* (broccoli) cultivar Saga with a 1 min treatment in 70% ethanol, followed by 15 min in 1.3% sodium hypochlorite with ca. 0.001% Alconox detergent. Seeds were grown in sterile plastic containers at a density of approximately 8 seeds/cm<sup>2</sup> for 72 hours on a 0.7% agar support that did not contain added nutrients. The environment was carefully controlled with broad spectrum fluorescent lighting, humidity and temperature control (16 hours light, 25°C / 8 hours dark, 20°C). The plants were rapidly and gently collected from the surface of the agar to minimize glucosinolate hydrolysis by endogenous myrosinase released upon plant wounding. A large quantity of sprouts was harvested by immediately and rapidly plunged into approximately 3 volumes of boiling water in order to inactivate endogenous myrosinase as

well as to extract glucosinolates and isothiocyanates from the plant tissue. Water was returned to a boil and maintained at a rolling boil for 3 min. Following the boiling step, sprouts were homogenized directly in their infusion water for 1 min using a Brinkman Polytron Homogenizer and the preparations were frozen at -79°C until use.

Inducer potential of plant extracts, prepared as described above, was determined by the microtiter plate bioassay method as described above. Inducer potential is nearly all due to glucosinolates; predominantly glucoraphanin, which is the glucosinolate of sulforaphane, but some glucoerucin which is the sulfide analog of glucoraphanin was also present. When converted to isothiocyanates by the addition of purified myrosinase, Phase 2 enzyme-inducing potential was 100,000 units/ml and contained 5.2  $\mu$ mol of isothiocyanates per ml, as determined by the cyclocondensation reaction described in Example 7. Thus, the subjects consumed a total of 520  $\mu$ mol of glucosinolates.

Collection of 8 hour urine samples was continued for an additional 30 hours. Urinary excretion of isothiocyanate conjugates (dithiocarbamates) was monitored using the cyclocondensation reaction as described in Example 7.

00113857,0720093

41

TABLE 5  
EXCRETION OF DITHIOCARBAMATES BY TWO SUBJECTS  
INGESTING 520 MICROMOLES OF GLUCOSINOLATES  
EXTRACTED FROM SAGA BROCCOLI

5

TIME	CONDITION	SUBJECT 1	SUBJECT 2
Collection Time (hours)		$\mu$ mol Dithiocarbamate per 8 hour urine collection	
8	baseline	1.4	2.7
16	baseline	2.1	0.9
24	baseline	1.7	5.4
32	1st 8 hour post-dose	23.2	20.4
40	2nd 8 hour post-dose	9.9	36.8
48	3rd 8 hour post-dose	4.4	14.0
56	4th 8 hour post-dose	4.2	4.1
Total post-dose minus average baseline:		39.8	63.2
Total as Percent of dose:		6.7%	12.2%

10

15

20 The two subjects studied metabolically converted a significant fraction of the ingested glucosinolates to the isothiocyanates which were converted to cognate dithiocarbamates and measured in the urine.

CL  
CLY/CL  
Example 12

EFFECTS OF PHYSICAL INTERVENTIONS ON SPROUT GROWTH  
ON PRODUCTION OF INDUCERS OF QUINONE REDUCTASE

25 Sprouts were prepared by first surface sterilizing seeds of *Raphanus sativum* (daikon) by a 1 minute treatment with 70% ethanol, followed by a 15 min treatment with 1.3% sodium hypochlorite with approximately 0.001% Alconox detergent. Seeds were grown

42

in sterile plastic containers at a density of approximately 8 seeds/cm<sup>2</sup> for 7 days on a 0.7% agar support that did not contain added nutrients. The environment was carefully controlled with broad spectrum fluorescent lighting, humidity and temperature control (16 hours light 25°C/8 hours dark, 20°C).

09418867-072098  
Treated sprouts were irradiated with germicidal UV light for 0.5 hr on days 5 and 6. Treated sprouts were only half the height of the untreated controls. Plants were harvested on day 7 by rapidly and gently collecting the plants from the surface of the agar to minimize glucosinolate hydrolysis by endogenous myrosinase released upon plant wounding. Sprouts were harvested by immediate and rapid plunging into approximately 10 volumes of DMF/ACN/DMSO (1:1:1) at approximately -50°C in order to inactivate endogenous myrosinase as well as to extract glucosinolates and isothiocyanates. Sprouts were immediately homogenized with a ground glass mortar and pestle and stored at -20°C.

Inducer potential of plant extracts, prepared as described above, was determined by the microtiter plate bioassay method as described above. Inducer potential of the UV-treated sprouts was over three times that of untreated controls. Treatment of sprouts with ultraviolet light therefore increased the Phase 2 enzyme-inducer potential of the plant tissue.

Although the foregoing refers to particular preferred embodiments, it will be understood that the present invention is not so limited. It will occur to those of ordinary skill in the art that various modifications may be made to the disclosed embodiments and that such modifications are intended to be within the scope of the present invention, which is defined by the following claims. All publications and patent applications mentioned in this specification are indicative of the

43

level of skill of those in the art to which the invention  
pertains.

5 All publications and patent applications are herein  
incorporated by reference to the same extent as if each  
individual publication or patent application were  
specifically and individually indicated to be  
incorporated by reference in its entirety.

09118867-072098

44



What Is Claimed Is:

1. Cruciferous sprouts, with the exception of cabbage, cress, mustard and radish sprouts, harvested prior to the 2-leaf stage.

2. The cruciferous sprouts according to claim 1, wherein said sprouts are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemmafera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selenisia*.

3. The cruciferous sprouts according to claim 2, wherein said sprouts are a *Brassica oleracea* variety *italica*.

4. The cruciferous sprouts according to claim 1, wherein said sprouts are a *Brassica oleracea* variety *botrytis*.

5. The cruciferous sprouts according to claim 1, wherein said sprouts are a *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

6. The cruciferous sprouts according to claim 1, wherein said sprouts are substantially free of Phase 1 enzyme-inducing potential.

7. A non-toxic solvent extract of the cruciferous sprouts according to claim 1.

8. The non-toxic solvent extract according to claim 7, wherein said solvent is water.

9. The non-toxic solvent extract according to claim 8, further comprising a cruciferous vegetable comprising an active myrosinase enzyme.

09113867-072098

45

10. The non-toxic solvent extract according to claim 9, wherein said cruciferous vegetable is of the genus *Raphanus*.

11. A method of increasing the chemoprotective amount of Phase 2 enzymes in a mammal, comprising the step of administering an effective quantity of the cruciferous sprouts according to claim 1.

12. Cruciferous sprouts harvested prior to the 2-leaf stage, wherein said sprouts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates.

13. The cruciferous sprouts according to claim 12, wherein said sprouts are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemmifera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selensia*.

14. The cruciferous sprouts according to claim 13, wherein said sprouts are a *Brassica oleracea* variety *italica*.

15. The cruciferous sprouts according to claim 13, wherein said sprouts are a *Brassica oleracea* variety *botrytis*.

16. The cruciferous sprouts according to claim 15, wherein said sprouts are a *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

17. A non-toxic solvent extract of the cruciferous sprouts according to claim 12.

00118867-072008

18. The non-toxic solvent extract according to claim 17, wherein said solvent is water.

19. The non-toxic solvent extract according to claim 18, further comprising a cruciferous vegetable comprising an active myrosinase enzyme.

20. The non-toxic solvent extract according to claim 19, wherein said cruciferous vegetable is of the genus *Raphanus*.

21. A method of preparing a food product rich in glucosinolates, comprising germinating cruciferous seeds, with the exception of cabbage, cress, mustard and radish seeds, and harvesting sprouts prior to the 2-leaf stage, to form a food product comprising a plurality of sprouts.

22. The method according to claim 21, wherein said sprouts contain non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates.

23. The method according to claim 21, wherein said seeds are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemnifera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selensia*.

24. The method according to claim 23, wherein said seeds are *Brassica oleracea* variety *italica*.

25. The method according to claim 23, wherein said seeds are *Brassica oleracea* variety *botrytis*.

26. The method according to claim 25, wherein said seeds are *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

09118867 0720090

27. A food product rich in glucosinolates made by the process according to claim 21.

28. A method of preparing a food product, comprising extracting glucosinolates and isothiocyanates from cruciferous sprouts according to claim 1 with a non-toxic solvent, removing the extracted sprouts from said solvent, and recovering the extracted glucosinolates and isothiocyanates.

29. A method of preparing a food product according to claim 28, wherein active myrosinase enzyme is mixed with said cruciferous sprouts, or said extracted glucosinolates and isothiocyanates, or both said cruciferous sprouts or said extract.

30. A method of preparing a food product rich in glucosinolates, comprising germinating cruciferous seeds that produce sprouts having at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth and which contain non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates, and harvesting sprouts prior to the 2-leaf stage to form a food product comprising a plurality of sprouts.

31. The method according to claim 30, wherein said seeds are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemmifera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selensia*.

32. The method according to claim 31, wherein said seeds are *Brassica oleracea* variety *italica*.

33. The method according to claim 31, wherein said seeds are *Brassica oleracea* variety *botrytis*.

09418867, 072009

34. The method according to claim 33, wherein said seeds are *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

35. A food product rich in glucosinolates, made by the process according to claim 30.

36. A method of preparing a food product, comprising introducing cruciferous seeds, wherein said seeds produce sprouts having at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates, into another edible ingredient.

37. A method of preparing a food product, comprising extracting glucosinolates and isothiocyanates with a non-toxic solvent and isothiocyanates from cruciferous seeds, sprouts, plants or plant parts wherein seeds that produce said sprouts, plant, or plant parts, have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth and wherein said seeds, sprouts, plants or plant parts have non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates, and recovering the extracted glucosinolates and isothiocyanates.

38. A method of preparing a food product according to claim 37, wherein active myrosinase enzyme is mixed with said cruciferous seeds, sprouts or plants; or said extracted glucosinolates and isothiocyanates; or both said cruciferous seeds, sprouts or plants and said extract.

39. A method of reducing the level of carcinogens in a mammal, comprising administering to a mammal an

09118867 072008

effective amount of cruciferous sprouts, with the exception of cabbage, cress, mustard and radish sprouts.

40. A method of reducing the level of carcinogens in a mammal, comprising administering to a mammal an effective amount of cruciferous sprouts having at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates.

41. A method of extracting glucosinolates and isothiocyanates from plant tissue comprising the steps of homogenizing said plant tissue in an excess of a mixture of dimethyl sulfoxide, acetonitrile and dimethylformamide at a temperature sufficient to inactivate myrosinase enzyme activity.

42. A food product comprising cruciferous sprouts, with the exception of cabbage, cress, mustard and radish sprouts, harvested prior to the 2-leaf stage, cruciferous seeds; extracts of said sprouts or seeds; or any combination of said sprouts, seeds or extracts.

43. A method of increasing the chemoprotective amount of Phase 2 enzymes in a mammal, comprising the step of administering an effective quantity of the food product according to claim 42.

44. A food product comprising cruciferous sprouts harvested prior to the 2-leaf stage, wherein said sprouts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts and non-toxic levels of indole glucosinolate and goitrogenic hydroxybutenyl glucosinolates; cruciferous seeds; extracts of said sprouts or seeds; or any combination of said sprouts, seeds or extracts.

09118867, 072098

50

45. A method of increasing the chemoprotective amount of Phase 2 enzymes in a mammal, comprising the step of administering an effective quantity of the food product according to claim 44.

46. Cruciferous sprouts harvested prior to the 2-leaf stage, wherein the ratio of monofunctional to bifunctional inducers is at least 20 to 1.

47. A food product supplemented with a purified or partially purified glucosinolate.

00140867 1072008  
000220 29887100

Add B<sub>1</sub>  
Add C<sub>2</sub>

Docket No. 46528/102/JOHO**DECLARATION AND POWER OF ATTORNEY**

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**CANCER CHEMOPROTECTIVE FOOD PRODUCTS**

the specification of which (check one)

- ☒ is attached hereto
- ☐ was filed on \_\_\_\_\_ as Application Serial No. \_\_\_\_\_ and was amended on \_\_\_\_\_ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

**PRIOR FOREIGN APPLICATION(S)**

NUMBER	COUNTRY	DAY/MONTH/YEAR FILED	PRIORITY CLAIMED

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations § 1.56, which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION SERIAL NO.	FILING DATE	STATUS: PATENTED, PENDING, ABANDONED

I hereby appoint as my attorneys, with full powers of substitution and revocation, to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: Stephen A. Bent, Reg. No. 29,768; David A. Blumenthal, Reg. No. 26,257; John J. Feldhaus, Reg. No. 28,822; Donald D. Jeffery, Reg. No. 19,980; Eugene M. Lee, Reg. No. 32,039; Peter G. Mack, Reg. No. 26,001; Brian J. McNamara, Reg. No. 32,789; Sybil Meloy, Reg. No. 22,749; George E. Quillin, Reg. No. 32,792; Colin G. Sandercock, Reg. No. 31,298; Bernhard D. Saxe, Reg. No. 28,665; Richard L. Schwaab, Reg. No. 25,479; Arthur Schwartz, Reg. No. 22,115; Harold C. Wegner, Reg. No. 25,258.

Send all correspondence to FOLEY & LARDNER, 3000 K Street, N.W., Suite 500, Washington, DC 20007-5109. Address telephone communications to Bernhard D. Saxe at (202) 672-5300.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of First or Sole Inventor <b>Jed W. FAHEY</b>	Signature of First or Sole Inventor <i>Jed W. Fahey</i>	Date <b>9/13/95</b>
Residence Address <b>6704 RIDGE RD., ELDERSBURG, MD 21784</b>	Country of Citizenship <b>United States</b>	
Post Office Address <b>6704 RIDGE RD., ELDERSBURG, MD 21784</b>		

Signatures should conform to names as typewritten. ☒ Additional inventors on attached Page 2.



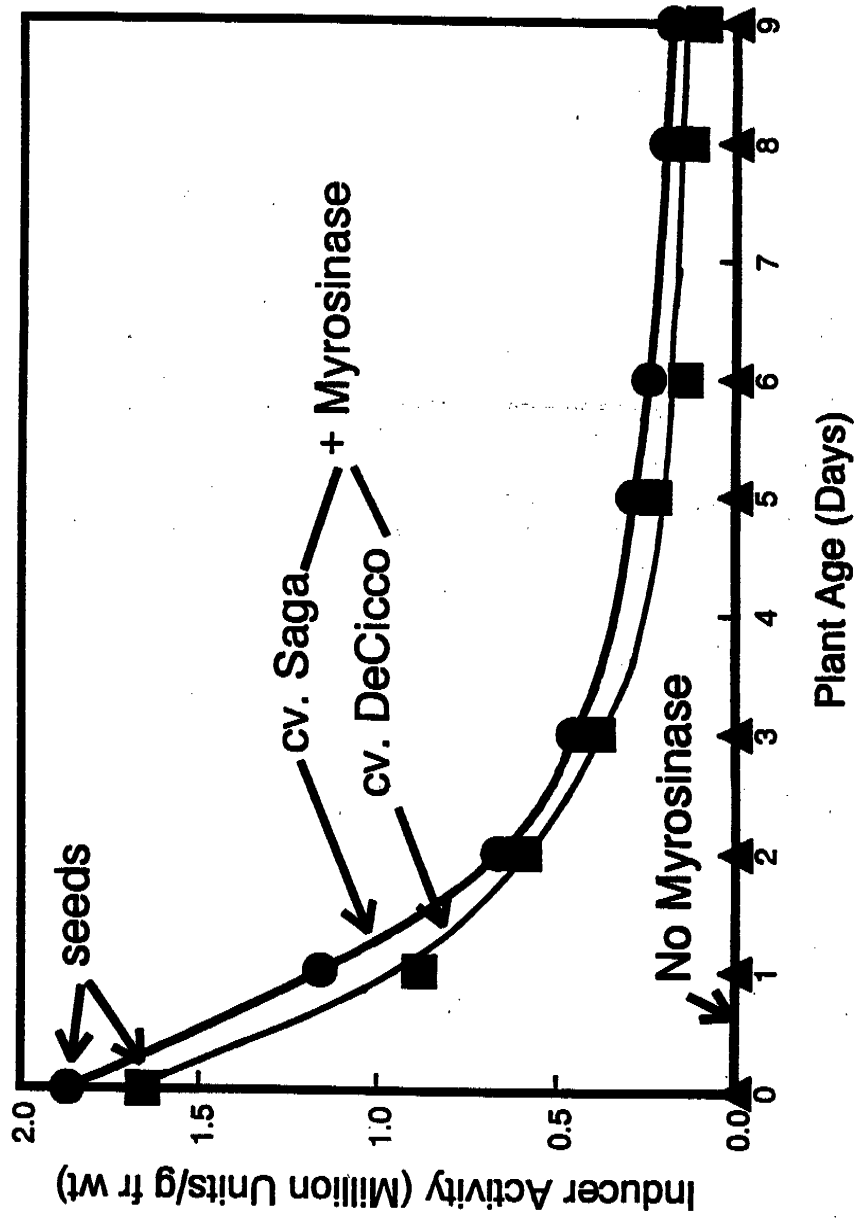
PAGE 2

Docket No. 46528/102/10HO

Full Name of Second Inventor <i>Paul TALALAY</i>	Signature of Second Inventor <i>Paul Talalay</i>	Date <i>9/13/95</i>
Residence Address <i>5512 BOXHILL LANE, BALTIMORE MD</i> <i>21210</i>	Country of Citizenship <i>United States</i>	
Post Office Address <i>5512 BOXHILL LANE BALTIMORE MD 21210</i>		

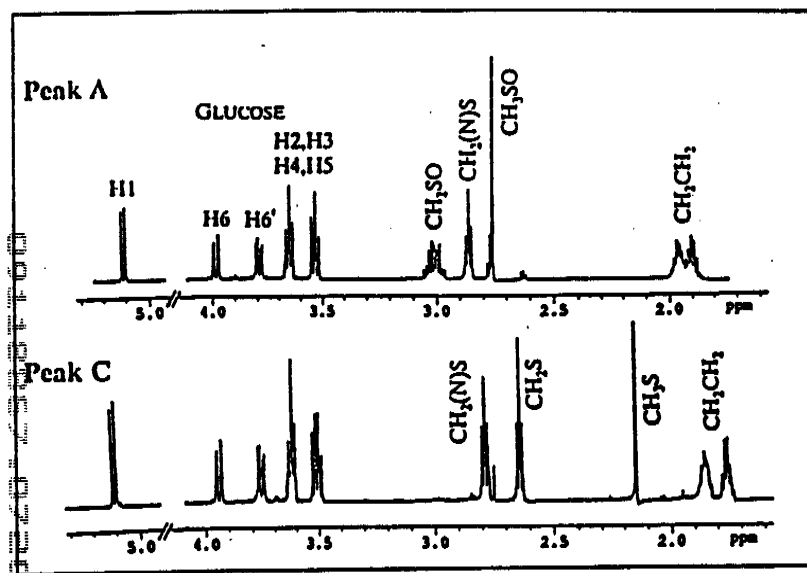
00118867 072098  
050220 1998T20

# Inducer Activity of Broccoli Sprouts Effect of Plant Age



▲ = < 1000 Units/g fr wt

Figure 1



High Resolution NMR (600 MHz) in D<sub>2</sub>O. Note: chirality of SO in Peak A induces multiplet for CH<sub>2</sub>SO (Peak A), not observed for CH<sub>2</sub>S (Peak C).

Figure 2

# Inducer Activity of Broccoli Sprouts

## Effect of Plant Age

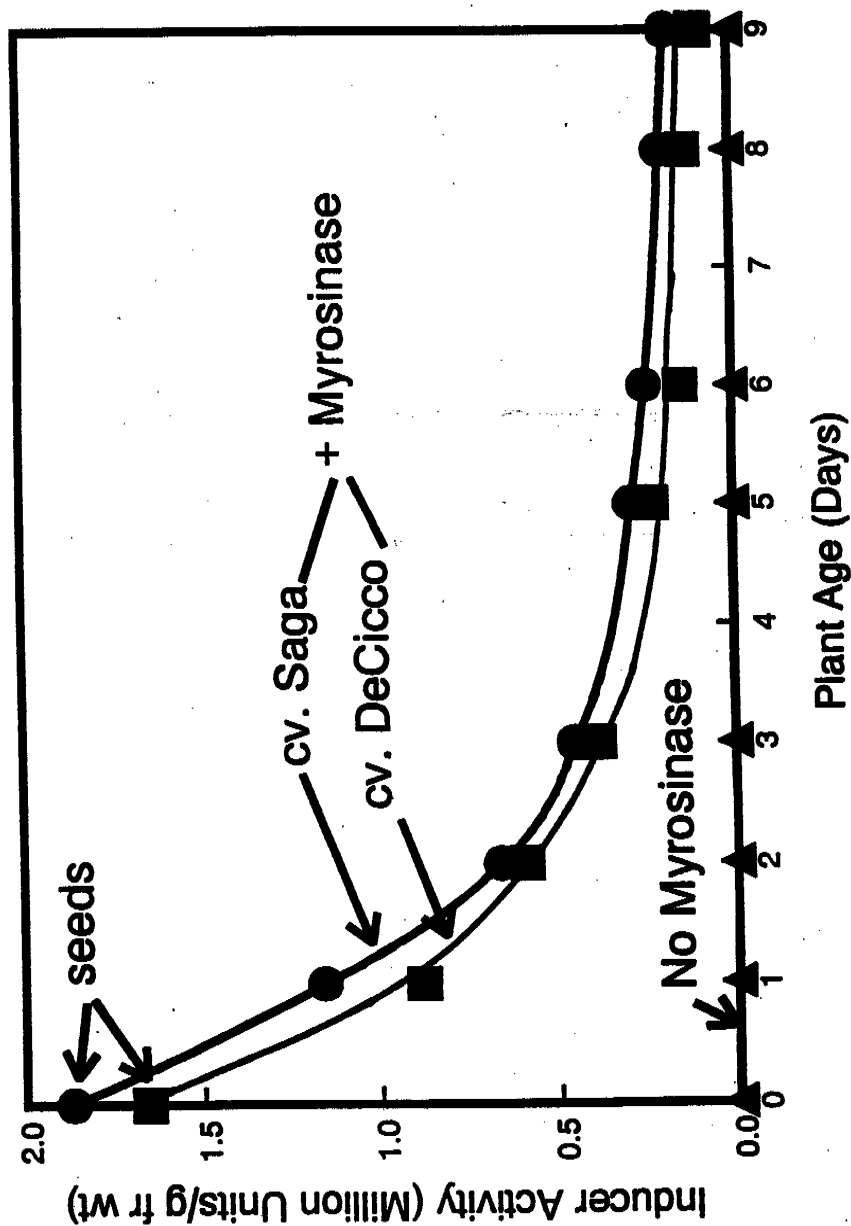
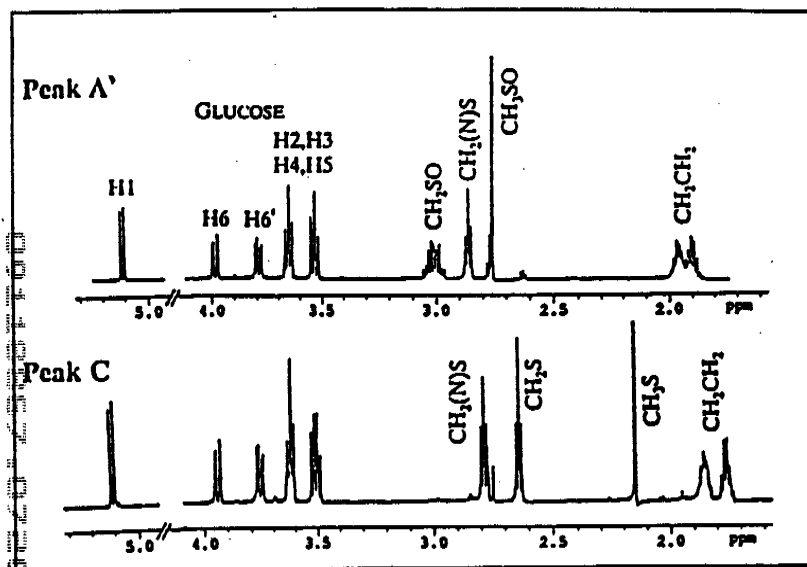


Figure 1



High Resolution NMR (600 MHz) in D<sub>2</sub>O. Note: chirality of SO in Peak A induces multiplet for CH<sub>2</sub>SO (Peak A), not observed for CH<sub>2</sub>S (Peak C).

Figure 2

Law Offices  
FOLEY & LARDNER

Suite 500  
3000 K Street, N.W.  
Washington, DC 20007-5109  
(202) 672-5300

07/20/98  
16408 U.S. PTO

Assistant Commissioner for Patents  
Box Patent Applications  
Washington D.C. 20231

U.S. PTO  
29811/60  
07/20/98

Attorney Docket No. 046528/0118

(must include alphanumeric codes if no inventors named)

**UTILITY PATENT APPLICATION TRANSMITTAL**  
(new nonprovisional applications under 37 CFR 1.53(b))

Transmitted herewith for filing is the patent application of:

INVENTOR(S): Jed W. FAHEY and Paul TALALAY

TITLE: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

In connection with this application, the following are enclosed:

**APPLICATION ELEMENTS:**

xx Specification - 51 TOTAL PAGES

(preferred arrangement:)

- Descriptive Title of the Invention
- Cross Reference to Related Applications
- Statement Regard Fed sponsored R&D
- Reference to Microfiche Appendix
- Background of the Invention
- Brief Summary of the Invention
- Brief Description of the Drawings (if filed)
- Detailed Description
- Claim(s)
- Abstract of the Disclosure

xx Drawings - Total Sheets 2

xx Declaration and Power of Attorney - Total Sheets 2

xx Newly executed (original or copy)

xx Copy from a prior application (37 CFR 1.63(d))

(relates to continuation/divisional boxes completed) - NOTE: Box below

xx DELETION OF INVENTOR(S) - Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).

xx Incorporation By Reference (useable if copy of prior application Declaration being submitted)

The entire disclosure of the prior application, from which a COPY of the oath or declaration is supplied as noted above, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

xx Microfiche Computer Program (Appendix)

xx Nucleotide and/or Amino Acid Sequence Submission (if applicable, necessary)

- xx Computer Readable Copy
- xx Paper Copy (identical to computer copy)
- xx Statement verifying identify of above copies

**ACCOMPANYING APPLICATION PARTS**

- xx Assignment Papers (cover sheet & document(s))
- xx 37 CFR 3.73(b) Statement (when there is an assignee)
- xx English Translation Document (if applicable)
- xx Information Disclosure Statement (IDS) with PTO-1449. xx Copies of IDS Citations
- xx Preliminary Amendment
- xx Return Receipt Postcard (MPEP 503)

Utility Patent Application Transmittal  
 Attorney Docket No. 528/0118 - Foley & Lardner  
 Page 2

- ☒ Small Entity Statement(s)  
☒ Statement file in prior application, status still proper and desired.  
☐ Certified Copy of Priority Document(s) with Claim of Priority  
 (if foreign priority is claimed).  
☐ OTHER:

If a **CONTINUING APPLICATION**, check appropriate box and supply the requisite information:

- ☐ Continuation ☒ Divisional ☐ Continuation-in-part (CIP)  
 of prior application Serial No. 08/840,234.

☒ Amend the specification by inserting before the first line the following sentence: --This application is a ☒ continuation, ☒ divisional or ☐ continuation-in-part of application Serial No. 08/840,234, filed April 11, 1997, in now US Patent 5,968,567, and a divisional application of 08/528,858, filed September 15, 1995, now US Patent 5,925,893

**CORRESPONDENCE ADDRESS:**

Foley & Lardner Address noted above.  
 Telephone: (202) 672-5300  
 Fax Number: (202) 672-5399

**FEE CALCULATIONS:** (Small entity fees indicated in parentheses.)

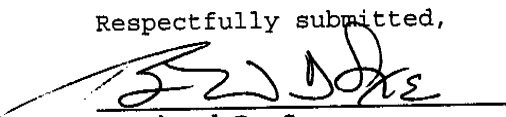
(1) For	(2) Number Filed	(3) Number Extra	(4) Rate	(5) Basic Fee \$790 (\$395)
Total Claims	21 - 20 =	1	x \$22 (x \$11)	11.00
Independent Claims	3 - 3 =	0	x \$82 (x \$41)	0.00
Multiple Dependent Claims			\$270 (\$135)	0.00
Assignment Recording Fee per property			\$40	0.00
Surcharge Under 37 C.F.R. 1.16(e)			\$130 (\$65)	0.00
TOTAL FEE:				\$406.00

**METHOD OF PAYMENT:**

A check in the amount of the above TOTAL FEE is attached. If payment by check is NOT enclosed, it is requested that the Patent and Trademark Office advise the undersigned of the period of time within which to file the TOTAL FEE. If payment enclosed, this amount is believed to be correct; however, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 19-0741.

Respectfully submitted,

Date: July 20, 1998  
 Docket No.: 046528/0118

  
 Bernhard D. Saxe  
 Reg. No. 28,665

#3/B

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 046528/0118

In re patent application of

Jed FAHEY *et al.*

Serial No. Unassigned

Filed: July 20, 1998

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination of the above-identified application, Applicants respectfully request that the following amendments be entered into the application:

IN THE CLAIMS:

Kindly cancel claims 1-47 without prejudice or disclaimer and add the following claims:

--48. Cruciferous sprouts, with the exception of *Brassica oleracea capitata*, *Lepidium sativum*, *Sinapis alba*, *Sinapis nigra*, and *Raphanus sativus* sprouts, harvested between the onset of germination up to and including the 2-leaf stage.

49. The cruciferous sprouts according to claim 48, wherein said sprouts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates and are harvested 1 to 14 days post-germination.

50. The cruciferous sprouts according to claim 48, wherein said sprouts are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*,

B,  
Sub C



Attorney Docket No. 16585/0118

*botrytis, costata, gemmifera, gongylodes, italica, medullosa, palmifolia, ramosa, sabauda, sabellica, and selensia.*

51. The cruciferous sprouts according to claim 50, wherein said sprouts are a *Brassica oleracea* variety *italica*.

52. The cruciferous sprouts according to claim 50, wherein said sprouts are a *Brassica oleracea* variety *botrytis*.

53. The cruciferous sprouts according to claim 50, wherein said sprouts are a *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

54. The cruciferous sprouts according to claim 48, wherein said sprouts are substantially free of Phase 1 enzyme-inducing potential.

55. A non-toxic solvent extract of the cruciferous sprouts according to claim 48.

56. The non-toxic solvent extract according to claim 55, wherein said solvent is water.

57. The non-toxic solvent extract according to claim 56, further comprising a cruciferous vegetable comprising an active myrosinase enzyme.

58. The non-toxic solvent extract according to claim 57, wherein said cruciferous vegetable is of the genus *Raphanus*.

59. The cruciferous sprouts according to claim 54, wherein the ratio of monofunctional to bifunctional Phase 2 enzyme inducers is at least 20 to 1.

60. A food product comprising the cruciferous sprouts according to claim 48, optionally including cruciferous seeds; extracts of said sprouts or seeds; or any combination of said sprouts, seeds or extracts.

Attorney Docket N 046585/0118

61. The food product according to claim 60, wherein said sprouts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts.

62. A food product rich in glucosinolates made by the process of germinating cruciferous seeds, with the exception of cabbage, cress, mustard and radish seeds, and harvesting sprouts between the onset of germination up to and including the 2-leaf stage, to form a food product comprising a plurality of sprouts.

63. The food product according to claim 62, wherein said sprouts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates and are harvested 1 to 14 days post-germination.

64. The food product according to claim 63, wherein said sprouts are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemnifera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selenisia*.

65. The food product according to claim 64, wherein said sprouts are *Brassica oleracea* variety *italica*.

66. The food product according to claim 64, wherein said sprouts are *Brassica oleracea* variety *botrytis*.

67. The food product according to claim 64, wherein said sprouts are *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

68. A food product supplemented with a purified or partially purified glucosinolate.--

00141075-072000

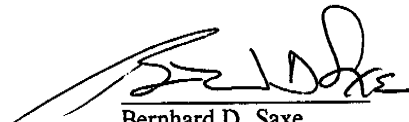
Attorney Docket No. 3585/0118

REMARKS

Claims 48-68 are now pending. Claims 1-47 have been canceled. New claims 48-68 have been added. Support for the new claims can be found in the original claims and the specification as filed. Entry of the foregoing amendment prior to examination is respectfully requested.

Respectfully submitted,

July 20, 1998

  
Bernhard D. Saxe  
Reg. No. 28,665

FOLEY & LARDNER  
3000 K Street, N.W.  
Suite 500  
Washington, D.C. 20007-5109  
Tel: (202) 672-5300

00110867 072008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of : Group Art Unit: 1761

Jed FAHEY et al.

Atty. Dkt. No. 46585/118

Serial No.: 09/118,867

JAN 12 1999

Filed: July 20, 1998

GROUP 1800

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

RECEIVED

INFORMATION DISCLOSURE STATEMENT

UNDER 37 C.F.R. §§1.56, 1.97(c) and 1.17(p)

JAN 14 1999

GROUP 1700

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

Included with the attached Form PTO-1449 are documents known to applicants in order to comply with applicants' duty of disclosure pursuant to 37 C.F.R. §1.56.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or is considered to be material to patentability as defined in 37 C.F.R. §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a prima facie prior art reference against the claims of the present application.

CONCISE EXPLANATION OF  
RELEVANCE OF EACH DOCUMENT

Applicants are submitting herewith on Form PTO-1449 a listing of the documents cited by or submitted to the Patent and Trademark Office in parent Application Serial Nos. 08/528,858 and 08/840,234, filed September 15, 1995, and April 11, 1997, respectively. The relevance of these documents is explained in the parent applications.

As provided in 37 C.F.R. §1.98(d), copies of the documents are not being provided since they were previously cited by or submitted to the Patent Office in the parent applications.

- 1 -

46528/118

Since this Information Disclosure Statement is being filed prior to the issuance of an Office Action, no fee is required in connection with its filing.

Applicants respectfully request that the listed documents be considered by the Examiner and be made of record in the present application and that an initialled copy of Form PTO-1449 be returned in accordance with M.P.E.P. §609.

Respectfully submitted,

January 13, 1999  
Date

Richard C. Peet  
Richard C. Peet  
Reg. No. 35,792

FOLEY & LARDNER  
3000 K Street, NW, Suite 500  
Washington, DC 20007-5109  
(202) 672-5300

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of : Group Art Unit: 1761  
 Jed FAHEY et al. : Dkt. No. 46585/118  
 Serial No.: 09/118,867  
 Filed: July 20, 1996  
 For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. §§1.56, 1.97(c) and 1.17(p) JAN 12 1999

Assistant Commissioner for Patents  
 Washington, DC 20231

GROUP 1700

Sir:

Included with the attached Form PTO-1449 is a documents known to applicants in order to comply with applicants' duty of disclosure pursuant to 37 C.F.R. §1.56.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or is considered to be material to patentability as defined in 37 C.F.R. § 1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* prior art reference against the claims of the present application.

The instant Information Disclosure Statement is being filed in compliance with 37 C.F.R §1.97(b) within three months of the filing date of the above-identified application.

As Applicants are in compliance with 37 C.F.R. §1.97(b), it is respectfully requested that the listed documents be considered by the Examiner and formally be made of record in the present application and that an initialled copy of modified Form PTO-1449 be returned in accordance with M.P.E.P. §609.

Respectfully submitted,

January 11, 1999  
 Date

Richard C. Peet  
 Richard C. Peet  
 Reg. No. 35,792

FOLEY & LARDNER  
 3000 K Street, NW, Suite 500  
 Washington, DC 20007-5109  
 (202) 672-5300

JAN 12 1999  
 GROUP 1800

Sheet <u>1</u> of <u>1</u>		FORM PTO-1449 (modified)		ATTY DOCKET NO. 46585/118		SERIAL NO. 09/118,867	
U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE				JAN 12 1999			
LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)				APPLICANT Jed FAHEY et al.		GROUP 1800	
Date Submitted to PTO: January 11, 1999				FILING DATE July 20, 1998		GROUP 1761	
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						
	AL						
	AM						
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
	BA						
	BB						
OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)							
EVA	CA	S. Meyerowitz	Sprout It! One Week From Seed to Salad, Steve Meyerowitz (The Sprout House, Inc., Great Barrington, MA), pages 20-21, 58, 85-86, 120-123, 1993.				
	CB		RECEIVED JAN 12 1999				
	CC		GROUP 1700				
EXAMINER <i>[Signature]</i>				DATE CONSIDERED <i>2/00</i>			

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

PT-212(a):4/90

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of

Jed FAHEY et al.

Serial No.: 09/118,867

Filed: July 20, 1998

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

Group Art Unit: 1761

Atty. Dkt. No. 046585/0118



REQUEST FOR CORRECTED FILING RECEIPT

The Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

RECEIVED

FEB 16 1999

MATRIX CUSTOMER  
SERVICE CENTER

Sir:

It is respectfully requested that a corrected Filing Receipt be issued in connection with the above-identified application in order to include --A Divisional of Application Serial No. 08/840,234, filed April 11, 1997--. Also, please change Attorney Docket No. "046528/0118" to -046585/0118--.

A copy of the Filing Receipt is enclosed. Kindly forward a corrected Filing Receipt to the undersigned attorney of record as soon as possible.

Respectfully submitted,

January 25, 1999  
Date

Richard C. Peet  
Richard C. Peet  
Reg. No. 35,792

FOLEY & LARDNER  
3000 K Street, NW, Suite 500  
Washington, DC 20007-5109  
(202) 672-5300

002.182785.1



PT 103X  
(Rev. 8-95)

## FILING RECEIPT



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTORNEY DOCKET NO.	DRWGS	TOT CL	IND CL
09/118,867	07/20/98	1761	\$406.00	046528/0118	2	21	3

046585/0118

FOLEY & LARDNER  
3000 K STREET NW STE 500  
WASHINGTON DC 20007-5109

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Application Processing Division's Customer Correction Branch within 10 days of receipt. Please provide a copy of the Filing Receipt with the changes noted thereon.

## Applicant(s)

JED W. FAHEY, ELDERSBURG, MD; PAUL TALALAY, BALTIMORE, MD.

FOREIGN FILING LICENSE GRANTED 08/13/98

\* SMALL ENTITY \*

## TITLE

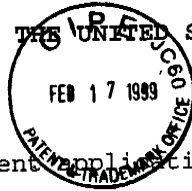
CANCER CHEMOPROTECTIVE FOOD PRODUCTS

PRELIMINARY CLASS: 426

--A Divisional of Application Serial No. 08/840,234, filed  
April 11, 1997--.

(see reverse)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Attorney Docket No. 046585/0118

In re patent application of  
FAHEY et al.

Group Art Unit: 1761

Serial No. 09/118,867

Examiner: UNKNOWN

Filed: July 20, 1998

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. § 1.56

Assistant Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

**RECEIVED**

**FEB 18 1999**

**GROUP 1700**

Sir:

Submitted herewith on Form PTO-1449 is a listing of documents known to applicants in order to comply with applicants' duty of disclosure pursuant to 37 C.F.R. § 1.56. A copy of the listed documents is being submitted to comply with the provisions of 37 C.F.R. § 1.97-1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or is considered to be material to patentability as defined in 37 C.F.R. § 1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a prima facie prior art reference against the claims of the present application.

**RECEIVED**

**FEB 24 1999**

**MATRIX CUSTOMER  
SERVICE CENTER**

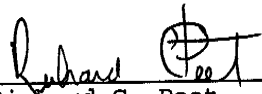
Serial No. 09/118,867

CONCISE EXPLANATION OF  
RELEVANCE OF EACH DOCUMENT

Applicants respectfully request that the listed documents be considered by the Examiner and be made of record in the present application and that an initialled copy of Form PTO-1449 be returned in accordance with M.P.E.P. § 609.

Respectfully submitted,

February 17, 1999  
Date

  
Richard C. Peet  
Reg. No. 35,792

FOLEY & LARDNER  
Suite 500  
3000 K Street, N.W.  
Washington, DC 20007-5109  
(202) 672-5300



Sheet <u>1</u> of <u>5</u>		FORM PTO-1449 (modified)		ATTY DOCKET NO. 46528/118		SERIAL NO. 09/118,867	
U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE				APPLICANT FAHEY <i>et al.</i>			
LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)				FILING DATE January 13, 1999		GROUP 1761	
Date Submitted to PTO: January 13, 1999							
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
KH	A1	5,411,986	05/1995	Cho et al.	514	514	—
KH	A2	5,725,895	03/1998	Fahey et al.	426	49	—

**3-C46**

[illegible]

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered.  
Include copy of this form with next communication to applicant.

[illegible]

**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



[illegible]

**\*EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.